Commentary

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Journal of Clinical Epigenetics
ISSN 2472-1158

2017
Vol.3 No.S2:43

DOI: 10.21767/2472-1158.100077

The Attachment Theory Today: From the Epigenetic Effects of Maternal Behavior to Psyco-Neuro-Endocrino-Immunology

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Citation: Spinelli M, Bonacini OE, Curati G, Birocco N, Surbek D (2017) The Attachment Theory Today: From the Epigenetic Effects of Maternal Behavior to Psyco-Neuro-Endocrino-Immunology. J Clin Epigenet. Vol.3 No.S2:43

Received: November 15, 2017; **Accepted:** December 04, 2017; **Published:** December 07, 2017

Commentary

Since centuries, philosophers and scientist have intensively discussed about the reciprocal role of “nature” and “culture” in influencing the numerous aspects of human development, including both biological - i.e. health or illness, body weight or life expectancy, etc... , and social factors – i.e. personality and attitudes, relations, social position etc...- . During the last decades, studies on monozygotic twins, separated at birth and grown up in different social and geographic environments, have brought further light in this so interesting but also challenging field, that encompasses at least six disciplines including phsycology, genetic, biology, neurology endocrinology and immunology.

From the view of psycologists, a prominent role is played by “culture”, and in general the post-natal family setting, that will provide the main “direction” of the developing-line of individual features [1]. Conversely, geneticists and biologists provide the contrasting evidence that any personal characteristic, including eventually also attitudes and personality, is rather merely due to specific DNA sequences, belonging to that individual, recognizing the brain as the key force to evolution, independently of direct environmental factors [1]. Although the fighting between these two paradigms gives honour to the study of human development, in that it shows how dynamic, challenging and complex it is, the emergent field of epigenetics is slowly but irreversibly going to unify these different perspectives, offering a new, intriguing and holistic vision of the human development [2].

The Advent of Epigenetic

Conrad Waddington coined the term epigenetics in the early 1940s [3], referring to ‘‘the branch of biology which studies the causal interactions between genes and their products which bring the phenotype into being” [4]. In the original sense of this definition, epigenetics referred to all molecular pathways modulating the expression of a genotype into a particular phenotype. Over the following years, with the rapid growth of genetics, the semantic field of the word has gradually re-modelled, referring currently to ‘‘the study of changes in gene function that are mitotically and/or meiotically heritable and that do not entail a change in DNA sequence'', [5,6]. One of the most investigated of these changes is DNA methylation. This chemical binding acts as a “footprint” that impairs any transcriptional factor to bind the appropriate region in order to let the expression of the downstream gene. In other word, the information contained in that gene is hidden and not more available. Conversely, the de-methylation of gene regions favours gene expression [7]. In other words, DNA methylation causes certain genes to be “turned on or off ” as a mechanical starter [8-11].

As an example of such changes in gene function but not in the DNA sequence, experiments in mice show how important a mother's diet can be in modelling these functional changes – that determine the so called epigenome - of her offspring. One of the most studied genes in mice is that called agouti. In normal mice, the agouti gene is methylated. Phenotypically, this leads to specific features, in that the coat colour is brown and the mouse has a low risk of developing obesity and its consequences

including diabetes and cancer. Conversely, when a mouse's agouti gene is completely unmethylated, its coat is yellow and it is more prone to obesity, diabetes and cancer. Despite the different phenotype, fat yellow mice and skinny brown mice remain genetically identical. However, the fat yellow mice are different because they have an epigenetic "mutation", or a different – and, in this case, pathological - epigenetic "footprint".

Thanks to the contribution of these "pivotal" experiments, the field of epigenetics rapidly widespread, diffusing the concept that genetic sequence is not set in stone and environmental factors can alter the expression of certain genes [9,12].

Clinical Implications of Epigenetic

Given the extent of epigenetic reprogramming that occurs during gametogenesis and embryogenesis and the vulnerability of the process, it is not difficult to understand how alteration in reprogramming could be of clinical relevance. Since epigenetic remodelling may occur also during folliculogenesis and embryogenesis, any alteration of the physiological environment during these critical phases could lead to a different epigenetic "footprint" [13] In the light of these considerations; researchers have attempted to determine whether children conceived using assistive reproductive technology (ART) carry epigenetic reprogramming defects.

At the other extreme, an epigenetic change might result in a perceptible alteration later in life such as cancer, coronary heart disease, stroke, or diabetes. An increased risk of heart disease, stroke, and diabetes is associated with malnutrition in utero and low birth-weight [12]. Concerns have also been raised about the epigenetic status of tumour suppressors or fertility concerns in individuals exposed to environmental toxins.

What it is strongly emerging from the latest research, is the outstanding importance of the interaction between mothers and their offspring in determining epigenetic variations in their offspring's phenotypes. The results of the experiment of Meaney & Szyf [14], reveal a strong association between the different levels of care to the pups from their mothers and the relatively different temperaments later in the adulthood. Specifically, rats who had received a better care from their mothers grew up in a relaxed and sociable fashion and with a handled stress better than their attention deprived counterparts [9,11,14].

To exclude any genetic inflow that could have biased these results, the researchers switched the pups: they gave the baby rats from mothers that tended to be less attentive to more care-givers mothers. The results confirmed their hypothesis of the environmental shaping on the physiological or pathological phyco- bio-physical development. Indeed, regardless of the behaviour of the biological mother, the pups responded to the external stimuli in the adulthood with "social skills" conforms to the behaviour of their caregiver shortly after birth [8,9]. A further follow-up gene analysis revealed that the rats that received more maternal attention had a decrease in methyl makers of the genes associated with brain development, so the researchers concluded that the maternal care removed the methyl markers that would have otherwise caused their nervous temperament [8,9].

Epigenetic and Bowlby's Theory

Intriguingly the results of Meany's experiment appear very similar to John Bowlby's ethological theory of attachment. This theory was elaborated in 1969 and it has become a reference point for the subsequent research efforts in developmental psychology, as it brings light to understand and interpret how the infant-caregiver bond is related to the future development of the later life. Bowlby's ethological theory of attachment describes the development of attachment between the infant and their caregiver during the first two years of life. This relationship with the parents or the caregivers has its roots in the various set of signals that call the parent to the baby, being based on the infant's emotional tie to the caregiver, and is the basis on which the child develops successively the various response to the external stimuli that promotes survival: the human infant, like the pups is provided at birth with a set of behaviours that help keep the caregiver nearby in order to be protected and supported while exploring the environment.

The theory of attachment, as Bowlby himself underlined, is tightly imbricated with the evolutionary survival of the species, ensuring both safety and competence in order to adequately respond to the external stimuli (15). In the light of the recent finding in the epigenetic field, it can be argued that this spectrum of behaviours descripted by Bowlby is the consequence of the epigenetic footprint provided by mother to the offspring.

A Promising New Paradigm of Medicine

The last epigenetic findings have opened the possibility to look at human development from a revolutionary point of view, that has the potential to integrate psychology, as well as genetic and biological principles into a very environmentally based approach [9,15]. To adopt this holistic vision, it is necessary to better understand the dynamics of human development and to moving forward in both biologically and environmentally based disciplines.

This is the ultimate aim of an emerging new paradigm of Medicine, that is called Psyco-Neuro-Endocrino-Immmulogy, a new vision that is receiving increasing attention from the scientific community and may represent in the future years the opening key in the understanding the human development.

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